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Understanding the Economic Burden of Nonsevere Nocturnal Hypoglycemic Events: Impact on Work Productivity, Disease Management, and Resource Utilization

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ABSTRACT

Objective: Nonsevere hypoglycemic events are common and may occur in one-third of persons with diabetes as often as several times a week. This study's objective was to examine the economic burden of nonsevere nocturnal hypoglycemic events (NSNHEs). **Methods:** A 20-minute Web-based survey, with items derived from the literature, expert input, and patient interviews, assessing the impact of NSNHEs was administered in nine countries to 18 years and older patients with self-reported diabetes having an NSNHE in the past month. **Results:** A total of 20,212 persons were screened, with 2,108 respondents meeting criteria and included in the analysis sample. The cost of lost work productivity per NSNHE was estimated to be between \$10.21 (Germany) and \$28.13 (the United Kingdom), representing 3.3 to 7.5 hours of lost work time per event. A reduction in work productivity (presenteeism) was also reported. Compared with respondents' usual blood sugar monitoring practice, on average, 3.6 ± 6.6 extra tests were conducted in the week following the event at a cost of approximately \$87.1 per year. Additional costs were also incurred for doctor visits as well as medical care required because of falls or injuries incurred during the NSNHE for an annual cost of \$2,111.3 per person per year. When taking into consideration the multiple impacts of NSNHEs for the total sample and the frequency that these events occur, the resulting total annual economic burden was \$288,000 or \$127 per person per event. **Conclusions:** NSNHEs have serious consequences for patients. Greater attention to treatments that reduce NSNHEs can have a major impact on reducing the economic burden of diabetes.
Keywords: economic burden, nocturnal hypoglycemia, resource utilization, work productivity.

Introduction

Nonsevere hypoglycemic events are common in both type 1 and type 2 diabetes and may occur in approximately one-third of persons with diabetes, with frequency of events as often as several times a week [1]. These events can occur at any time of day or night while patients are at rest or engaged in activities [1–3]. These events represent a major challenge for both patients and clinicians, interfere with optimal long-term diabetes control, and contribute to excess morbidity and mortality [4–6]. In addition, nonsevere hypoglycemia has been shown to have an economic burden for patients, employers and health care payer systems [7], increased blood glucose (BG) monitoring, health care resource utilization, and patient out-of-pocket expenses [7,8].

In previous survey studies of both nighttime and daytime events, nonsevere nocturnal hypoglycemic events (NSNHEs), those occurring while sleeping, have been shown to potentially have a greater impact than daytime events on lost work productivity due to both absenteeism and presenteeism [7]. Furthermore, qualitative research has shown that nighttime events disrupt both sleep quality and quantity, resulting in impaired functioning and well-being the following day [8]. Thus, previous quantitative as well as qualitative research on NSNHEs has begun to suggest that these events are consequential contributors to increasing health care costs as well as the overall economic burden of diabetes [3,7,8]. The purpose of this study was to explore, in greater depth than has previously been done, the economic burden of these NSNHEs in terms of lost work productivity and health care resource utilization. This information is critical data that can be instrumental in helping to better understand, manage, and contain costs associated with these events and reduce the overall cost of care.

Methods

Survey Development and Conduct

A survey assessing the impact of NSNHEs was developed on the basis of the literature, expert input, and interviews with 78 persons with diabetes in nine focus groups in four countries (the United States, the United Kingdom, Germany, and France) who recently had experienced an NSNHE [8]. The survey items were developed on the basis of a qualitative analysis of the expert input and the persons with diabetes interviews and cognitively debriefed and pilot tested in English in nine persons who met the

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same eligibility criteria as the focus groups. These steps were conducted to ensure content validity (relevant questions) and to ensure that the questions had face validity with the respondents (e.g., no unfamiliar/strange words or concepts). The final questionnaire was translated into all relevant languages by using a forward and backward translation process [8]. The survey was administered via a secure Internet server in the United States, the United Kingdom, Germany, Canada, France, Italy, Spain, The Netherlands, and Sweden. Findings, based on the current survey regarding the impact of NSNHEs on daily functioning and diabetes management, have been previously published [9].

NSNHEs were defined for the respondent as "nighttime hypoglycemic episode that happened while you were sleeping and did not require medical attention (such as needing to call an ambulance, go to the emergency room/hospital) or did not require help from anyone else to manage the hypo. You knew that you were having this hypoglycemic episode because you had symptoms like sweating and/or confusion or perhaps you experienced no symptoms, but noted the hypoglycemic episode when measuring your blood sugar." Respondents were asked questions regarding reasons for the event, length of time of the event, impact on productivity, daily functioning, and well-being. The survey took approximately 20 minutes to complete, and respondents were remunerated US $3 to US $5 depending on country for completing the survey. The survey had several real-time validation steps (e.g., plausible min–max input values) and skip-patterns depending on the respondents' reply. Before database release, additional cross-checks were performed.

Sample

To be eligible to complete the survey, the respondent had to have a self-reported diagnosis of diabetes and experienced at least one NSNHE in the past month, be 18 years or older, and able to read the predominant language of the country he or she was living in. To ensure the generalizability of the results and reduce recruitment source bias, a multisource informant strategy was used. A multisource informant strategy is important when conducting correlational/regression-oriented research because it allows one to examine associations between predictors and outcomes when common method or source variance is not shared and enables researchers to rule out alternative explanations that would probably not be testable with single-source, single-method data sets [10,11]. The multisource informant strategy included a preconsented, online patient panel, e-mail recruitment, affiliate networks, and Web site advertising. Patients were recruited from more than 100 Web sites as well as from face-to-face and telephone surveys where appropriate to include members who were not frequent online users. Furthermore, all respondents were blinded to the purpose of the survey before entering the survey to reduce the possibility of self-identifying as a person with diabetes for the purpose of completing the survey. All respondents had either been identified as a person with diabetes and age 18 years or older in a prior blinded survey as a prerequisite of being a panel member (not related to this study) or, if not a member of the panel, by answering a blinded question asking about all their diagnoses and then being invited to enter the survey only if diabetes was listed as a diagnosis. In addition, the panel was constituted to be representative of the general population for age, sex, race, and income, and used for research only; panelists were not exposed to third-party advertising or direct marketing campaigns, nor were their personal data sold to third parties. The panel was also frequently refreshed to ensure that the panel was dynamic in nature and reflected any changes in the online population that might be occurring. Last, the incentive was low (~US $3–$5 depending on country) to help ensure that there was no undue incentive to participate in the panel. The incentive amount was set by the survey administrators on the basis of the length of the survey and historical knowledge of respondent expectations, and was consistent with honoraria given for similar surveys. Because of ethical considerations, the same honorarium was given to both panel and nonpanel respondents. For panel members, the honorarium was given as a "credit" that could be combined with "credits" from other surveys and redeemed at a later point in time.

The selection process used a sampling frame in a preexisting panel of persons with self-reported type 1 or type 2 diabetes. All respondents went through a health care profiler (screening questions) to ensure that a physician had diagnosed their diabetes and that a relevant treatment was initiated. A stratified sampling procedure used invitation selection criteria to account for disproportional response rates between stratification categories. Stratification variables were age (18–29 years, 30–49 years, 50–64 years, and ≥65 years), diabetes type (type 1 diabetes and type 2 diabetes), sex, and working status (working and nonworking).

Statistical Testing

Results by country are presented via frequencies or descriptives (means and SDs) with differences explored by using analysis of variance for continuous variables and Pearson chi-square for proportions. Statistical significance was tested between countries with the highest and lowest values. Responses for amount of work time lost contained outliers (>180 hours), or observations that appeared to be inconsistent with other observations in the data set. To account for these departures from normality, a 5% trim was used [12]. This trim was used for the analysis for calculating the cost of lost work productivity and resulted in two cases being dropped. The human capital approach using average wages to estimate productivity was used. To estimate input for the human capital method, an average of 36.8 working hours per week (corresponding to the self-reported working hours in Table 1) with an estimated 47 working weeks per year (a total of 1730 working hours per year) was used. The 2011 gross domestic product per capita was used as an estimate for annual income [13]. An estimated average income (in US $) of $29.79/h in the United States, $22.25/h in the United Kingdom, $23.34/h in Germany, $24.98/h in Canada, $21.64/h in France, $18.78/h in Italy, $18.84/h in Spain, $25.96/h in The Netherlands, and $24.86/h in Sweden was used to estimate the value of the lost productivity [13]. The estimated productivity loss per NSNHE because of absenteeism was calculated on the basis of the proportion of persons reporting missed work multiplied with the hourly income multiplied with the hours missed (e.g., for an NSNHE during working hours in the United States, 12.6% of the sample reported missing work for 3.5 hours at the cost of $29.79/h, which is approximately equal to $13.37 per event).

The costs for doctor visits (or other health care professional) were derived from in-country data (Spain [14], Italy [15], France [16], The Netherlands [17], Sweden [18], the United Kingdom [19], the United States [20], Canada [20], and Germany [21,22]). The costs were converted into US $ by using the International Monetary Fund exchange rate data on June 1, 2012 [23]. The costs per visit used to estimate the value of general practitioner visits were $40.66 (Spain), $28.34 (Italy), $28.34 (France), $34.50 (The Netherlands), $164.72 (Sweden), $47.50 (the United Kingdom), $65.51 (the United States), $65.51 (Canada), and $38.20 (Germany).

Presenteeism was assessed by using the Endicott Work Productivity Scale [24] as well as a patient-reported Likert scale assessment. The Endicott Work Productivity Scale is a 25-item measure assessing the impact of a disease/event on a person's ability to perform work functions due to behaviors and subjective feelings or attitudes (e.g., ability to concentrate or impatience or annoyance with others at work). For this survey, the response time frame asked respondents to rate the impact on their work the day following their last NSNHE. For the 0 to 10 scale rating “how much this hypo impacted productivity at work,” 0 represented “My hypo did not impact my productivity at work at all” and 10 represented “My hypo had an extremely negative impact on my productivity at work,” mirroring the standard interpretations of Cohen’s effect size [25] classifications of mild, moderate, and severe. Thus, mean scores were collapsed to “no impact (score 0), “a little impact” (scores 1–2), moderate impact (3–6), and high impact (scores 7–10).

Results

The Sample

A total of 20,212 respondents with self-reported diabetes were screened. Of these, 2,673 (13.2% prevalence) reported an NSNHE during the last month and were eligible for the study. Of those eligible, 2,108 completed the survey for a response rate of 78.9%. A little over half, 52.2% of the analytic sample (n = 1,100), reported working for pay. The sample was equally divided between men and women (49.8%/50.2%), with a mean age of 49.9 years. The mean diabetes duration was 13.7 years, and subjects reported approximately 2 comorbid conditions on average (ranging between 0 and 11 out of a possible list of 13 most common comorbid conditions). As per the stratified inclusion criteria, two-third (67.2%) of the sample had type 2 diabetes. The majority of the sample used insulin (74.2%), with the remainder on oral treatments only. The majority of the respondents (32.1%) reported experiencing an NSNHE at least several times a month (insulin = 33.7%, oral = 27.6%), 15.9% about once a week (insulin = 16.0%, oral = 15.8%), 7.7% not daily but more than once a week (insulin = 7.1%, oral = 9.6%), and 0.9% daily (insulin = 0.8%, oral = 1.1%). The rest of the sample (43.3%) reported having NSNHEs once a month to very rarely (insulin = 42.5%, oral = 45.9%). No significant differences in experience were found ($P = 0.063$) between patients in insulin and oral treatments or those with and without comorbidity. The overall recall period for when the event occurred was short, with 76.3% (n = 1609) reporting having an NSNHE within the last 2 weeks (insulin = 77.1%, oral = 74.2%) (Table 1).

Impact of NSNHE on Work Productivity

Of working respondents, 13.8% (n = 151) reported missing work time, of which 2.6% (n = 28) missed a full day and 11.2% (n = 123) missed partial day (either going late to work the next day or leaving early) because of the NSNHE. For those missing work, the average working time lost was 5.3 ± 11.8 hours. Patients on insulin also had a higher percentage of work absence (66.7%) than did those on oral treatment (33.3%) ($P = 0.076$).

Based on Endicott Work Productivity Scale scores, the impact of the NSNHE on presenteeism had a mean score of 21.3 ± 21.0, which is significantly higher than that for groups defined as normal controls in two recent studies (ranging from mean 3.54 [26] and mean 15.6 ± 11.7 to 18.2 ± 10.7 [27]), comparable to the score among patients with arthritis (mean = 21.5 ± 14.3) [28] and lower than the score among patients reporting psychiatric disorders (mean = 40.8 ± 21.6) [29]. Patients on insulin had a lower (better) score (mean = 19.2 ± 20.8) than did those on oral treatment (mean = 27.0 ± 21.0; $P < 0.001$).

For those who worked the next day, the impact of the previous night event was apparent, with 42.6% of the respondents reporting that they had trouble focusing or concentrating the next day at work, 20.1% not completing work tasks on time, and 15.6% needing to reschedule their work day. Twenty-five percent of the sample reported that the NSNHE had a high impact on productivity at work the following day, 32.1% reported moderate impact, 18.9% reported a little impact, and 24.0% reported no impact of the NSNHE on their work productivity (Table 2).

The total yearly cost of lost work productivity for the working sample (52% of total sample) due to working either a partial day or missing a full day of work, based on the number of reported events per month in the working sample, was estimated to be $520.4 (insulin = $452.7, oral = $586.0; $P = 0.277$) per working person. Costs per country varied significantly, ranging from $216.3 (Germany) to $1,171.5 (Italy) ($P < 0.002$).

Post hoc regression analyses using productivity at work questions as dependent variables showed that comorbidity did not have a significant impact on whether respondents “go late to work because of the hypo” or miss a full day/days of work because of the hypo. For those with greater comorbidity, however, NSNHEs did have a significantly greater, negative impact at work on their work productivity ($P < 0.001$) and resulted in leaving work early more often ($P = 0.01$) (Table 3).

Impact on Diabetes Management and Health Care Resource Utilization

There was an increase in health services utilization reported, with 14.8% (n = 313) of the respondents contacting a primary care doctor or clinic as a result of having an NSNHE, with subjects on orals only having a significantly higher contact rate than did those on insulin (22.3% vs. 12.3%, respectively, $P < 0.01$). In addition, of the 1,873 subjects who reported having an NSNHE that woke them up, 145 respondents (7.7%) tripped or fell as a result of the NSNHE, of which 31.0% (n = 45) hurt themselves, and of these 26.7% (n = 12) required a visit to a doctor or other health professional. Subjects on insulin reported fewer trips/falls than did subjects on orals only (6.1% vs. 9.2%, $P < 0.05$); however, there were no differences in who hurt themselves or who required a visit to a doctor.

Compared with respondents’ usual blood sugar monitoring practice, on average, 3.6 ± 6.6 extra tests were conducted in the week following the event, with no significant difference between those taking insulin (3.5 ± 6.8) and orals (3.9 ± 5.8). The estimated yearly health care utilization cost due to NSNHEs for increased BG monitoring was $87.1 ± 313.9, assuming $1 cost per BG monitoring strip. The estimated yearly cost for visits to health care providers for falls and trips resulting in injury was $2,111.3 per person who experienced a fall. The costs varied between countries, ranging from between $786 in the United States to the highest $10,203 in Italy. No test for significance was made because the variance between countries was too high (Table 4).

Total Economic Burden

When taking into consideration the multiple impacts of NSNHEs (lost work time assuming that 52% of the sample is working, increased diabetes management, and increased health service resource utilization) and the frequency that these events occur, the resulting total annual economic burden for this sample was $288,000 or $127 per person per event. The amounts by country, from lowest to highest, were $8,700 (Sweden), $13,335 (The Netherlands), $18,268 (Canada), $27,274 (Germany), $34,536 (the United Kingdom), $39,083 (Italy), $41,108 (France), $44,724 (the United States), and $46,620 (Spain).

Discussion

This study has confirmed that NSNHEs are not uncommon in patients with type 1 and type 2 and occur in the past month in

Table 1 – Sample demographic characteristics.

	Total	UK	Germany	USA	Canada	France	Italy	Spain	The Netherlands	Sweden	P
Sample size with NSNHE within last month (N)	2108	305	279	501	200	193	138	242	169	81	
Age (y), mean ± SD (range)	49.9 ± 13.6 (20–89)	48.4 ± 13.4 (20–81)	49.0 ± 13.6 (20–85)	53.7 ± 13.0 (20–89)	54.5 ± 12.6 (22–83)	45.9 ± 13.5 (20–83)	44.6 ± 12.5 (20–76)	42.2 ± 11.9 (20–77)	55.3 ± 11.2 (22–81)	54.7 ± 13.5 (23–81)	0.000*
Sex: female, n (%)	1059 (50.2)	153 (50.2)	123 (44.1)	300 (59.9)	120 (60.0)	89 (46.1)	56 (40.6)	105 (43.4)	76 (45.0)	37 (45.7)	0.000†
Type of diabetes, n (%)											0.000†
Type 1	692 (32.8)	109 (35.7)	88 (31.5)	122 (24.4)	50 (25.0)	83 (43.0)	75 (54.3)	75 (31.0)	44 (26.0)	46 (56.8)	
Type 2	1416 (67.2)	196 (64.3)	191 (68.5)	379 (75.6)	150 (75.0)	110 (57.0)	63 (45.7)	167 (69.0)	125 (74.0)	35 (43.2)	
Diabetes duration (y), mean ± SD (range)	13.7 ± 11.3 (0.1–75.6)	13.6 ± 11.8 (0.4–57)	11.8 ± 9.7 (0.1–49)	14.8 ± 11.8 (0.3–60.7)	14.4 ± 10.7 (0.3–48)	13.7 ± 11.0 (0.3–50.3)	14.2 ± 12.3 (0.1–75.6)	10.2 ± 8.5 (0.3–49.6)	14.0 ± 11.3 (1.4–70.3)	21.4 ± 14.3 (1.6–58.3)	0.000*
Number of medical complications, mean ± SD (range)	1.1 ± 1.2 (0–6)	1.0 ± 1.2 (0–6)	1.0 ± 1.0 (0–5)	1.4 ± 1.3 (0–6)	1.2 ± 1.2 (0–5)	0.9 ± 1.1 (0–5)	0.9 ± 1.0 (0–4)	0.9 ± 1.0 (0–5)	1.0± 1.0 (0–4)	1.0 ± 1.3 (0–5)	0.000*
Diabetes treatment, n (%)											0.000†
Insulin	1565 (74.2)	210 (68.9)	226 (81.0)	351 (70.1)	139 (69.5)	156 (80.8)	106 (76.8)	164 (67.8)	135 (79.9)	78 (96.3)	
Orals	543 (25.7)	95 (31.1)	53 (19.0)	150 (29.9)	61 (30.5)	37 (19.2)	32 (23.2)	78 (32.2)	34 (20.1)	3 (3.7)	
Work for pay, n (%)											0.000†
Yes	1100 (52.2)	156 (51.1)	166 (59.5)	208 (41.5)	87 (43.5)	108 (56.0)	91 (65.9)	169 (69.8)	76 (45.0)	39 (48.1)	
No	1008 (47.8)	149 (48.9)	113 (40.5)	293 (58.5)	113 (56.5)	85 (44.0)	47 (34.1)	73 (30.2)	93 (55.0)	42 (51.9)	
Hours worked per week, mean ± SD	36.8 ± 11.0	33.7 ± 11.7	38.6 ± 11.6	36.5 ± 11.3	35.7 ± 10.7	38.2 ± 9.0	37.0 ± 9.2	40.2 ± 8.8	32.3 ± 13.2	35.3 ± 11.2	0.000*
Frequency of NSNHE,‡ n (%)											
All (type 1 and type 2) (N = 2108)											0.000†
Daily	18 (0.9)	1 (0.3)	3 (1.1)	4 (0.8)	1 (0.5)	4 (2.1)	2 (1.4)	3 (1.2)	0 (0.0)	0 (0.0)	
Not daily, but more than once a week	163 (7.7)	15 (4.9)	13 (4.7)	59 (11.8)	14 (7.0)	20 (10.4)	11 (8.0)	19 (7.9)	10 (5.9)	2 (2.5)	
About once a week	336 (15.9)	61 (20.0)	48 (17.2)	72 (14.4)	17 (8.5)	35 (18.1)	23 (16.7)	37 (15.3)	28 (16.6)	15 (18.5)	
Several times a month	677 (32.1)	88 (28.9)	88 (31.5)	164 (32.7)	70 (35.0)	71 (36.8)	48 (34.8)	82 (33.9)	50 (29.6)	16 (19.8)	
Once a month	414 (19.6)	59 (19.3)	69 (24.7)	85 (17.0)	28 (14.0)	32 (16.6)	28 (20.3)	43 (17.8)	41 (24.3)	29 (35.8)	
Only a few times a year	401 (19.0)	68 (22.2)	49 (17.6)	83 (16.6)	58 (29.0)	25 (13.0)	23 (16.7)	47 (19.4)	36 (21.3)	12 (14.8)	
Very rarely	99 (4.7)	13 (4.3)	9 (3.2)	34 (6.8)	12 (6.0)	6 (3.1)	3 (2.2)	11 (4.5)	4 (2.4)	7 (8.6)	
Type 1 (n = 692)											0.002†
Daily	8 (1.2)	0 (0.0)	3 (3.4)	0 (0.0)	0 (0.0)	2 (2.4)	2 (2.7)	1 (1.3)	0 (0.0)	0 (0.0)	
Not daily, but more than once a week	52 (7.5)	5 (4.6)	0 (0.0)	20 (16.4)	2 (4.0)	6 (7.2)	8 (10.7)	5 (6.7)	4 (9.1)	2 (4.3)	
About once a week	134 (19.3)	27 (24.8)	18 (20.5)	22 (18.0)	5 (10.0)	18 (21.7)	14 (18.7)	9 (12.0)	9 (20.5)	12 (26.0)	
Several times a month	232 (33.5)	32 (29.4)	26 (29.5)	42 (34.4)	22 (44.0)	33 (39.8)	24 (32.0)	30 (40.0)	14 (31.8)	9 (19.6)	
Once a month	141 (20.4)	19 (17.4)	24 (27.3)	18 (14.8)	11 (22.0)	14 (16.9)	13 (17.3)	11 (14.7)	12 (27.3)	19 (41.3)	
Only a few times a year	115 (16.6)	23 (21.1)	17 (19.3)	17 (13.9)	10 (20.0)	9 (10.8)	12 (16.0)	18 (24.0)	5 (11.4)	4 (8.7)	
Very rarely	10 (1.4)	3 (2.8)	0 (0.0)	3 (2.5)	0 (0.0)	1 (1.2)	2 (2.7)	1 (1.3)	0 (0.0)	0 (0.0)	
Type 2 (n = 1416)											0.003†
Daily	10 (0.7)	1 (0.5)	0 (0.0)	4 (1.1)	1 (0.7)	2 (1.8)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	

Table 1 – *continued*

	Total	UK	Germany	USA	Canada	France	Italy	Spain	The Netherlands	Sweden	P
Not daily, but more than once a week	111 (7.8)	10 (5.1)	13 (6.8)	39 (10.3)	12 (8.0)	14 (12.7)	3 (4.8)	14 (8.4)	6 (4.8)	0 (0.0)	
About once a week	202 (14.3)	34 (17.3)	30 (15.7)	50 (13.2)	12 (8.0)	17 (15.5)	9 (14.3)	28 (16.8)	19 (15.2)	3 (8.6)	
Several times a month	445 (31.4)	56 (28.6)	62 (32.5)	122 (32.2)	48 (32.0)	38 (34.5)	24 (38.1)	52 (31.1)	36 (28.8)	7 (20.0)	
Once a month	273 (19.3)	40 (20.4)	45 (23.6)	67 (17.7)	17 (11.3)	18 (16.4)	15 (23.8)	32 (19.2)	29 (23.2)	10 (28.6)	
Only a few times a year	286 (20.2)	45 (23.0)	32 (16.8)	66 (17.4)	48 (32.0)	16 (14.5)	11 (17.5)	29 (17.4)	31 (24.8)	8 (22.9)	
Very rarely	89 (6.3)	10 (5.1)	9 (4.7)	31 (8.2)	12 (8.0)	5 (4.5)	1 (1.6)	10 (6.0)	4 (3.2)	7 (20.0)	

Note. Data on ethnicity not available due to technical difficulty.
NSNHE, nonsevere nocturnal hypoglycemic event.
* Analysis of variance.
† Chi-square.
‡ About how often do you have nighttime hypo episodes (while you are sleeping) that do not require medical attention (such as needing to call an ambulance or go to the emergency room/hospital) or do not require help from anyone else to manage the hypo episode?

approximately 13.2% of the patients with frequency of events similar regardless of diabetes type (>50% at least monthly). Furthermore, although the incidence of hypoglycemic events may be lower for patients on orals than on insulin [30], randomized controlled trial studies have shown that rates may be as high as 38% for patients on oral treatments [31]. As shown in this study, however, for those patients who do have NSNHEs, the frequency of these events is similar to that of patients on insulin. There was also no difference in the frequency of events for those with less comorbidity. Patients on orals, however, as well as those with a fewer number of comorbidities, did report a lower impact on work productivity and less work absenteeism due to NSNHEs. This suggests that for this subset of patients, the consequences of the event may be less for those with less comorbidity or on oral treatment only. This evidence should further dispel the myth that nonsevere events are a concern only to patients with type 1 diabetes.

The longer term impacts of these events such as poor concentration last far longer than the immediate experience of the acute symptoms of the NSNHE (shaking, sweats, etc.) and can impact next-day functioning at work as well as daily functioning and well-being. Clearly, these events are "non-minor" or "non-severe," and labeling these events as such is a serious misnomer and may contribute to the lack of attention or appreciation of the importance of NSNHEs by a portion of clinicians. We suggest that calling these events "self-treated hypoglycemia" would be more accurate as well as less dismissive of their consequences.

The total economic burden of NSNHEs must include not only lost work productivity but also costs incurred for increased diabetes management and health care resource utilization. Using a human capital approach, the lost productivity per NSNHE was estimated in the range from $10.21 to $28.13 across all nine countries. The extrapolated yearly costs for these events are in the range of $216.3 to $1,171.5 per patient. With regard to increased diabetes management costs, however, the number of extra BG tests per NSNHE was estimated in the range from 1.8 to 6.8 across all countries, with an average yearly cost of $87.1 per person. In addition, increased health care utilization accounted for $2,111 per person in yearly costs due to falls resulting from the NSNHE. It should be noted, however, that only less than 1% of the population experienced falls and further research is needed to understand these costs in a larger sample. The total yearly cost for all reasons as a result of NSNHEs is estimated to be $288,000 for this sample. Furthermore, these costs may be an underestimation for three reasons. First, the full extent of the economic burden of these NSNHEs on work productivity does not include the impact of the NSNHE on the ability to be productive at work (presenteeism) and the cost of reduced focus or concentration at work. Second, the increased health care resource utilization costs due to additional contacts with health care providers (additional phone calls or questions to health care providers reported in this survey by 14.8% of the respondents) could not be estimated because of lack of information on parameters (e.g., length) of the contact. In addition, because it was not known whether those who missed work because of an event were hourly or salaried workers, this may have impacted their ability or willingness to miss work time because of the event. Last, the total economic burden as a result of the NSNHE should also include the additional out-of-pocket costs of the individual patient to manage these events. This was not assessed in this study although previous studies have found these costs to be consequential; the average dollar amount spent per year per person to manage nonsevere hypoglycemic events was $25/month for purchases such as increased number of glucose monitoring strips or food purchases more substantial than just a sugar packet or juice [7].

It is of note that the impact of NSNHEs on work productivity (presenteeism) is similar to that of arthritis, a major debilitating

Table 2 – Impact of an NSNHE on work productivity.

	Total	UK	Germany	USA	Canada	France	Italy	Spain	The Netherlands	Sweden	P
NSNHE, Working for pay N (with 5% trim)*	N = 1098	N = 155	N = 166	N = 207	N = 87	N = 108	N = 91	N = 169	N = 76	N = 39	
How much did hypo impact productivity at work (0 = no impact; 10 = extremely negative impact), mean ± SD	3.8 ± 3.1	4.5 ± 3.1	3.6 ± 3.1	3.4 ± 3.1	4.4 ± 3.2	3.9 ± 3.0	3.2 ± 2.9	3.8 ± 2.9	3.7 ± 3.0	2.5 ± 3.0	0.001†
Missing work time (late to work/leave early/miss full day), n (%)	151 (13.8)	26 (16.8)	22 (13.3)	26 (12.6)	15 (17.2)	16 (14.8)	11 (12.1)	20 (11.8)	7 (9.2)	8 (20.5)	0.663‡
If missing work time, what was the amount of work time lost (late to work/leave early/miss full day) (h), mean ± SD	5.3 ± 11.8	7.5 ± 15.7	3.3 ± 5.5	3.5 ± 10.8	3.5 ± 3.3	3.9 ± 8.7	5.7 ± 6.5	10.4 ± 20.7	5.6 ± 7.4	2.2 ± 2.5	0.538†
Because of the hypo, did you: n (%)											
Postpone work appointments	68 (6.2)	11 (7.1)	13 (7.8)	12 (5.8)	9 (10.3)	7 (6.5)	4 (4.4)	7 (4.1)	2 (2.6)	3 (7.7)	0.518‡
Reschedule work day	171 (15.6)	21 (13.5)	30 (18.1)	20 (9.7)	16 (18.4)	20 (18.5)	11 (12.1)	35 (20.7)	12 (15.8)	6 (15.4)	0.141‡
Have difficulty focusing or concentrating at work	468 (42.6)	81 (52.3)	86 (51.8)	83 (40.1)	39 (44.8)	41 (38.0)	34 (37.4)	62 (36.7)	30 (39.5)	12 (30.8)	0.013‡
Not complete work tasks and/or activities in a timely manner	221 (20.1)	41 (26.5)	26 (15.7)	47 (22.7)	21 (24.1)	17 (15.7)	8 (8.8)	40 (23.7)	13 (17.1)	8 (20.5)	0.022‡
Feel people at work noticed you were experiencing effects of the hypo from the night before	167 (15.2)	33 (21.3)	18 (10.8)	34 (16.4)	13 (14.9)	17 (15.7)	11 (12.1)	29 (17.2)	5 (6.6)	7 (17.9)	0.113‡

NSNHE, nonsevere nocturnal hypoglycemic event.
* The top 5% was trimmed for these results. This dropped two subjects (one from the USA and one from the UK).
† Analysis of variance.
‡ Chi-square.

Table 3 – The economic cost of lost work productivity due to NSNHEs.

	Total	UK	Germany	USA	Canada	France	Italy	Spain	The Netherlands	Sweden
NSNHE, Working for pay N (with 5% trim)*	N = 1098	N = 155	N = 166	N = 207	N = 87	N = 108	N = 91	N = 169	N = 76	N = 39
Work absenteeism										
Data regarding the last NSNHE										
Missing work time (late work/leave early/miss full day), n (%)	151 (13.8)	26 (16.8)	22 (13.3)	26 (12.6)	15 (17.2)	16 (14.8)	11 (12.1)	20 (11.8)	7 (9.2)	8 (20.5)
Hourly income (US $)	23.38	22.25	23.34	29.79	24.98	21.64	18.78	18.84	25.96	24.86
The amount of work time lost (late work/leave early/miss full day) (h), mean ± SD	5.3 ± 11.8	7.5 ± 15.7	3.3 ± 5.5	3.5 ± 10.8	3.5 ± 3.3	3.9 ± 8.7	5.7 ± 6.5	10.4 ± 20.7	5.6 ± 7.4	2.2 ± 2.5
Cost of productivity loss per event (US $)	17.14	28.13	10.21	13.37	14.89	12.60	12.98	23.14	13.38	11.12
Lost work productivity (for subsample who reported missing work time)										
Estimated yearly lost productivity per person										
Event frequency of NSNHEs per year, mean†	30	20.4	21.6	36	20.4	31.2	91.2	21.6	16.8	21.6
Productivity loss of an NSNHE (US $)‡	520.4	578.7	216.3	488.0	303.2	395.0	1171.5	507.9	219.8	248.1

NSNHE, nonsevere nocturnal hypoglycemic event.

* The top 5% was trimmed for these results. This dropped two subjects (one from the USA and one from the UK).

† Mean calculated for subjects who indicated "missing work time"; the mean estimated yearly events was based on their reported frequency of events where daily = 360, not daily but more than once per week = 104, about once a week = 52, several times a month = 24, and once a month = 12.

‡ Calculated by multiplying the number of events by the cost of productivity loss per cost.

Table 4 – Medical resource utilization after the last NSNHE.

	Total (N = 2108)	UK (N = 305)	Germany (N = 279)	USA (N = 501)	Canada (N = 200)	France (N = 193)	Italy (N = 138)	Spain (N = 242)	The Netherlands (N = 169)	Sweden (N = 81)	P
Number of extra blood sugar tests after the last NSNHE, mean ± SD											
1st day (day of the NSNHE)	1.3 ± 1.5	1.3 ± 1.4	1.3 ± 1.3	1.1 ± 1.3	1.4 ± 1.6	1.1 ± 1.4	1.4 ± 1.2	1.8 ± 1.9	1.3 ± 1.4	1.0 ± 1.2	0.000*
2nd day	0.6 ± 1.2	0.6 ± 1.1	0.5 ± 1.0	0.4 ± 0.9	0.8 ± 1.4	0.6 ± 1.1	0.9 ± 1.1	1.1 ± 1.6	0.5 ± 1.1	0.2 ± 0.7	0.000*
3rd day	0.4 ± 1.0	0.4 ± 1.0	0.3 ± 0.9	0.3 ± 0.8	0.5 ± 1.2	0.5 ± 1.0	0.6 ± 1.0	0.9 ± 1.6	0.3 ± 0.9	0.1 ± 0.7	0.000*
4–7 d	1.3 ± 3.6	1.1 ± 3.3	0.8 ± 2.9	0.8 ± 2.7	1.4 ± 4.0	1.5 ± 3.9	1.6 ± 3.3	3.0 ± 5.5	0.9 ± 2.6	0.5 ± 2.4	0.000*
Total (7 d after the NSNHE)	3.6 ± 6.6	3.4 ± 6.1	3.0 ± 5.5	2.5 ± 5.0	4.2 ± 7.5	3.8 ± 6.8	4.5 ± 6.1	6.8 ± 10.0	3.0 ± 5.3	1.8 ± 4.2	0.000*
Contacted a health care professional after the last NSNHE, n (%)											
Yes†	313 (14.8)	36 (11.8)	61 (21.9)	40 (8.0)	29 (14.5)	33 (17.1)	35 (25.4)	58 (24.0)	16 (9.5)	5 (6.2)	0.000‡
Falls and trips											
Did you trip and/or fall during this nighttime hypo? Yes, n (%)§	145 (7.7)	25 (9.4)	23 (9.9)	27 (6.2)	6 (3.4)	21 (12.1)	8 (6.2)	25 (11.5)	5 (3.1%)	5 (6.5%)	0.003‡
When you trip/fall, did you hurt yourself? Yes, n (%)	45 (31.0)	12 (48.0)	1 (4.3)	7 (25.9)	0 (0.0%)	7 (33.3)	2 (25.0)	12 (48.0)	3 (60.0)	1 (20.0)	0.011‡
Did this trip/fall require a visit to doctor or other health professional? Yes, n (%)	12 (26.7)	4 (33.3)	0 (0.0)	1 (14.3)	–	1 (14.3)	1 (50.0)	4 (33.0)	0 (0.0)	1 (100)	0.493‡
Estimated yearly cost for falls per person (US $)	2,111.3	1,282.4	–	786.1	–	1,360.3	10,202.6	975.9	–	3,253.3	–

NSNHE, nonsevere nocturnal hypoglycemic event.

* Analysis of variance.

† Primary care doctor, hospital, diabetes clinic, other.

‡ Chi-square.

§ Data on falls were calculated on the subjects who reported having an NSNHE that woke them up (n = 1873).

disease with a major impact on patient functioning and well-being as well as economic costs of care [32–35]. In addition, the estimated yearly economic burden of these events is slightly less than the yearly economic burden of influenza (372 million) in the United States [36].

This survey also identified a previously undiscussed economic impact of NSNHEs, namely, falls or injuries due to the event. Falls and subsequent visits to health care providers are both frightening to patients and represent an additional health care cost. Given that the elderly are more prone to falls [37], that the prevalence of diabetes increases with age [38], and that there is a 47% increased risk of recurrent falls in this cohort [39], one can assume that the economic burden for this population is even greater than for younger persons with diabetes. In addition, it was unknown whether these respondents also had orthostatic hypotension, which may have contributed as a risk factor for falling. Further research is needed to better understand the prevalence and economic implications for these falls and injuries as a consequence of NSNHEs.

As expected, country differences were found. The samples in The Netherlands and Germany seem to have a lower economic burden (in terms of cost) than the samples in other countries. Respondents from the United Kingdom and Spain reported higher global costs, while Italy had the highest per person costs dealing with their NSNHEs. The higher costs for Italy may have been driven by the smaller sample size in which a higher proportion of respondents reported a higher frequency of NSNHEs than did respondents in other countries. Furthermore, one person in Italy who reported a health care visit due to a fall also reported a daily frequency of NSNHEs. This high frequency and related costs may represent a unique case.

Several limitations with this study should be mentioned. First, the response rate for the survey was 78.9% and although this can be considered a very high response rate, it is feasible that some response bias may have been introduced because of nonresponders. Because of ethical considerations, no information was collected on nonresponders because they did not sign an informed consent form. Therefore, comparison of responders and nonresponders for characteristics that may have introduced nonresponder bias was not possible. Furthermore, accuracy of reporting, as with any survey, is a consideration because recall bias may have influenced findings. Recall of episodes of NSHEs, however, up to a week can be considered relatively accurate [40], and recall of longer durations was considered to be accurate as reported by focus group participants in the groups conducted to generate items for this survey. The recall period for most of the sample (76.3%) was within the last 2 weeks, and no recall period was longer than 1 month. Given the self-report nature of this data, some respondents may have overestimated or underestimated variables such as income or age or misrepresented their diagnosis. This bias should be recognized as a potential bias in all studies using self-reported data. The minimal honoraria for completing the survey, as well as the fact that respondents recruited via panels were already preidentified on some of the variables that may have been misrepresented (e.g., age and income), however, may have reduced the risk of this potential bias. Also, as in all research, there may be a potential bias of collecting data only from persons who choose to participate in research. The fact that this study collected data via an Internet-based survey may also introduce a selection bias in the respondents who were able to participate (i.e., only literate respondents with access to a computer). The proportion of Internet users in all nine countries based on total population (including infants and the very old), however, is high (highest in Sweden, 92%, to lowest in Italy, 47.7%). We suspect that Internet usage is higher for the predominant age group relevant in this study (18–64 years). Moreover, the rate of literacy is high in all nine countries (99% in most countries, with lowest in Spain, 97.7%) [13]. Accuracy may be impacted by any incentives given to the respondents for completion of the survey. In this study, the amount of the incentive was minimal (~US $3–$5 depending on country), which we believe would not have affected responses or decisions to participate in the study. Furthermore, all countries that participated in the study were North American or Western European countries where the similarities in diabetes care can be considered to outweigh the differences. It is unclear whether in countries with more distinct medical systems, cultures, or diabetes management pathways, a similar study would yield the same results. Last, given the panel nature of the survey, it was not possible to have a physician-confirmed diagnosis. It was not known, however, to the patients who completed the screener beforehand that only those with diabetes would be administered the survey. In the screener, the subjects were provided with several medical conditions and asked to check which they had been diagnosed with by a physician. Only those who checked diabetes, among the multiple possibilities, were invited to complete the full survey. It is possible that some patients did misrepresent their diagnosis; however, given the small honorarium incentive provided and the a priori known panel screening characteristics, we believe that this group was not large enough to influence findings.

Conclusions

In conclusion, this study strongly suggests that NSNHEs are significant events for patients and represent an important economic burden in terms of both lost work productivity and increased health care resource utilization across several countries. These events should not be considered “minor” or “non-severe,” and incorporating a discussion of these events and optimal corrective action strategies into all diabetes management treatment plans should facilitate reducing the economic burden of NSNHEs.

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